

WHAT IS CLAIMED IS:

1. A method of screening for a modulator of MCIP binding to calcineurin comprising:
  - (a) providing an MCIP and calcineurin;
  - (b) admixing the MCIP and calcineurin in the presence of a candidate modulator;
  - (c) measuring MCIP/calcineurin binding; and
  - (d) comparing the binding in step (c) with the binding of MCIP and calcineurin in the absence of said candidate modulator,whereby a difference in the binding of MCIP and calcineurin in the presence of said candidate modulator, as compared to binding in the absence of said candidate modulator, identifies said candidate modulator as a modulator of MCIP binding to calcineurin.
2. The method of claim 1, wherein MCIP and calcineurin are part of a cell free system.
3. The method of claim 1, wherein MCIP and calcineurin are located within an intact cell.
4. The method of claim 3, wherein said cell is a myocyte.
5. The method of claim 3, wherein said cell is a H9C2 cell, a C2C12 cell, a 3T3 cell, a 293 cell, a neonatal cardiomyocyte cell or a myotube cell.
6. The method of claim 3, wherein said intact cell is located in a animal.
7. The method of claim 1, wherein said modulator increases MCIP binding to calcineurin.

8. The method of claim 1, wherein said modulator decreases MCIP binding to calcineurin.
9. The method of claim 1, wherein either or both MCIP and calcineurin are labeled.
10. The method of claim 9, wherein both MCIP and calcineurin are labeled, one with a quenchable label and the other with a quenching agent.
11. The method of claim 9, wherein both MCIP and calcineurin are labeled, but said labels are not detectable unless brought into proximity of each other.
12. The method of claim 3, wherein said intact cell is engineered to overexpress MCIP, calcineurin or both.
13. The method of claim 1, wherein measuring comprises immunologic detection of MCIP, calcineurin or both.
14. The method of claim 1, further comprising measuring binding of MCIP and calcineurin in the absence of said modulator.
15. The method of claim 1, wherein MCIP is MCIP1.
16. The method of claim 1, wherein MCIP is MCIP2.
17. The method of claim 1, wherein MCIP is MCIP3.
18. A method of screening for a modulator of MCIP dephosphorylation comprising:
  - (a) providing a phosphorylated MCIP and calcineurin;
  - (b) admixing the MCIP and calcineurin in the presence of a candidate modulator;
  - (c) assessing MCIP phosphorylation; and
  - (d) comparing the phosphorylation state of MCIP in step (c) with the phosphorylation state of MCIP in the absence of the candidate modulator,

whereby a difference in MCIP phosphorylation in the presence of said candidate modulator, as compared to phosphorylation in the absence of said candidate modulator, identifies said candidate modulator as a modulator of MCIP phosphorylation.

19. The method of claim 18, wherein MCIP and calcineurin are part of a cell free system.
20. The method of claim 19, wherein MCIP and calcineurin are located within an intact cell.
21. The method of claim 20, wherein said cell is a myocyte.
22. The method of claim 20, wherein said cell is a H9C2 cell, a C2C12 cell, a 3T3 cell, a 293 cell, a neonatal cardiomyocyte cell or a myotube cell.
23. The method of claim 20, wherein said intact cell is located in a mammal.
24. The method of claim 18, wherein said modulator increases MCIP dephosphorylation by calcineurin.
25. The method of claim 18, wherein said modulator decreases MCIP phosphorylation by calcineurin.
26. The method of claim 18, wherein total phosphorylation is assessed.
27. The method of claim 20, wherein said intact cell expresses a protein selected from the group consisting of PKC, CaMK, GSK3 and MAPK and isoforms and variants thereof.
28. The method of claim 27, wherein said intact cell is engineered to overexpress one or more of MCIP and calcineurin.
29. The method of claim 18, wherein assessing comprises detection of radiolabeled phosphorus, detection of changes of electrophoretic mobility, or detection of binding by antibodies that discriminate between phosphorylation states.

30. The method of claim 18, further comprising assessing dephosphorylation of MCIP in the absence of said modulator.
31. The method of claim 18, wherein MCIP is MCIP1.
32. The method of claim 31, wherein phosphorylation at Ser108 is assessed.
33. The method of claim 18, wherein MCIP is MCIP2.
34. The method of claim 18, wherein MCIP is MCIP3.
35. A method of screening for a modulator of MCIP expression comprising:
  - (a) providing a cell expressing an MCIP and calcineurin;
  - (b) administering to said cell a candidate modulator;
  - (c) measuring MCIP expression; and
  - (d) comparing the expression in step (c) with the expression of MCIP in the absence of the candidate modulator,whereby a difference in MCIP expression in the presence of said candidate modulator, as compared to expression in the absence of said candidate modulator, identifies said candidate modulator as a modulator of MCIP expression.
36. The method of claim 35, wherein said cell is a myocyte.
37. The method of claim 36, wherein said myocyte is a cardiomyocyte.
38. The method of claim 35, further comprising measuring MCIP expression in the absence of the candidate modulator.
39. The method of claim 35, wherein measuring MCIP expression comprises assessing transcription by Northern analysis.

40. The method of claim 35, wherein measuring MCIP expression comprises assessing transcription by quantitative RT-PCR.
41. The method of claim 35, wherein measuring MCIP expression comprises ELISA.
42. The method of claim 35, wherein measuring MCIP expression comprises Western blot.
43. The method of claim 35, wherein said MCIP is selected from the group consisting of MCIP1, MCIP2 and MCIP3.
44. The method of claim 35, wherein said modulator increases MCIP expression.
45. The method of claim 35, wherein said modulator decreases MCIP expression.
46. A method of screening for a modulator of muscle cell growth comprising:
- (a) providing a cell expressing an MCIP and calcineurin;
  - (b) administering to said cell a candidate modulator;
  - (c) measuring transcription of a target molecule that is indicative of muscle cell growth; and
  - (d) comparing the transcription in step (c) with the transcription of the target molecule in the absence of the candidate modulator,
- whereby a difference in muscle cell growth in the presence of said candidate modulator, as compared to growth in the absence of said candidate modulator, identifies said candidate modulator as a modulator of muscle cell growth.
47. The method of claim 46, wherein said cell is a myocyte.
48. The method of claim 47, wherein said myocyte is a cardiomyocyte.
49. The method of claim 47, further comprising measuring transcription of the target molecule in the absence of the candidate inhibitor.
50. The method of claim 47, wherein said target molecule is MEF2.

51. The method of claim 47, wherein said MCIP is MCIP1.
52. The method of claim 47, wherein said MCIP is MCIP2.
53. The method of claim 47, wherein said MCIP is MCIP3.
54. The method of claim 47, wherein said modulator increases muscle cell growth.
55. The method of claim 47, wherein said modulator decreases muscle cell growth.
56. The method of claim 47, wherein said cell is located in a mammal.
57. A method of modulating muscle cell growth comprising:
- (a) providing a modulator of MCIP binding to calcineurin; and
  - (b) administering said modulator to a muscle cell,
- whereby administration of said modulator results in modulation of muscle cell growth.
58. A method of modulating muscle cell growth comprising:
- (a) providing a modulator of MCIP dephosphorylation by calcineurin; and
  - (b) administering said modulator to a muscle cell,
- whereby administration of said modulator results in modulation of muscle cell growth.
59. A method of modulating muscle cell growth comprising:
- (a) providing a modulator of MCIP expression; and
  - (b) administering said modulator to a muscle cell,
- whereby administration of said modulator results in modulation of muscle cell growth.
60. The method of claim 59, wherein said muscle cell is located in a mammal.

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61. The method of claim 59, wherein said ~~modulator~~ is an agonist of muscle cell growth.
62. The method of claim 61, wherein said agonist is a small molecule.
63. The method of claim 61, wherein said agonist is an expression construct comprising an expression cassette comprising a DNA segment encoding an MCIP operably linked to a promoter active in said muscle cell.
64. The method of claim 63, wherein said MCIP is MCIP1.
65. The method of claim 63, wherein said promoter is selected from the group consisting of myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter,  $\text{Na}^+/\text{Ca}^{2+}$  exchanger promoter, dystrophin promoter, creatine kinase promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter and atrial natriuretic factor promoter.
66. The method of claim 63, wherein said expression cassette further comprises a polyadenylation signal.
67. The method of claim 63, wherein said expression construct further comprises an origin of replication.
68. The method of claim 63, wherein said expression construct is a viral expression construct.
69. The method of claim 68, wherein said viral expression construct is selected from the group consisting of an adenoviral construct, a retroviral construct, an adeno-associated viral construct, a herpesviral construct, a vaccinia viral construct, a polyoma viral construct, and a Sindbis viral vector.
70. The method of claim 60, further comprising administering to said mammal a pharmaceutical agent used to treat cardiac disease.

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71. An isolated and purified DNA segment encoding a MCIP1 promoter.
72. An MCIP1 promoter isolatable from the sequence of SEQ ID NO:11.
73. An expression cassette comprising 50-1000 base pairs of SEQ ID NO:11 operably linked to a DNA segment encoding a polypeptide other than MCIP1.
74. The expression cassette of claim 73, wherein said polypeptide is screenable marker protein.
75. A host cell comprising an expression cassette comprising 50-1000 base pairs of SEQ ID NO:11 operably linked to a DNA segment encoding a polypeptide other than MCIP1.
76. A method for screening for modulators of MCIP1 expression comprising:
  - (a) providing a cell transformed with an expression cassette comprising 50-1000 base pairs of SEQ ID NO:11 operably linked to a DNA segment encoding a screenable marker protein;
  - (b) administering to said cell a candidate modulator;
  - (c) measuring expression of said marker protein; and
  - (d) comparing the expression of said marker protein in step (c) with the expression of said marker protein in the absence of said candidate modulator,

whereby a difference in marker protein expression in the presence of said candidate modulator, as compared to expression in the absence of said candidate modulator, identifies said candidate modulator as a modulator of MCIP expression.

77. A method of treating cardiac hypertrophy or heart failure comprising administering to a subject suffering from cardiac hypertrophy or heart failure an agent that promotes MCIP binding to calcineurin.



78. The method of claim 77, further comprising treating said subject with an ionotrope, a beta blocker, an antiarrhythmic, a diuretic, a vasodilator, a hormone antagonist, an endothelin antagonist, an angiotensin type 2 antagonist or a cytokine inhibitor/blocker.
79. The method of claim 77, wherein said agent is a phosphatase that acts on Ser108 of MCIP or an inducer of a phosphatase that acts on Ser108 of MCIP.
80. The method of claim 77, wherein said agent is a MCIP analogue that binds calcineurin but lacks a removable phosphate at Ser108.
81. The method of claim 77, wherein said agent is a small molecule.
82. The method of claim 77, wherein said agent is administered orally or intravenously.
83. The method of claim 77, wherein said agent is administered in a delayed release formulation.
84. The method of claim 77, wherein said agent is an expression cassette comprising an MCIP coding sequence under the control of a promoter active in cardiac tissue.
85. The method claim 84, wherein said promoter is a constitutive promoter.
86. The method of claim 84, wherein said promoter is an inducible promoter.
87. An isolated and purified nucleic acid encoding an MCIP1 polypeptide that lacks sequences encoded by Exons 1, 2 and 3.
88. The nucleic acid of claim 87, further comprising a promoter.
89. The nucleic acid of claim 88, wherein said promoter is a muscle specific promoter.
90. The nucleic acid of claim 89, wherein said muscle specific promoter is myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter,  $\text{Na}^+/\text{Ca}^{2+}$

exchanger promoter, dystrophin promoter, creatine kinase promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, and alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter and atrial natriuretic factor promoter.

91. The nucleic acid of claim 88, wherein said promoter is the native MCIP1 promoter.
92. The nucleic acid of ~~claim~~-87, further comprising an origin of replication.
93. The nucleic acid of ~~claim~~ 92, where said nucleic acid is a non-viral vector.
94. The nucleic acid of claim 92, wherein said nucleic acid is a viral vector.
95. An isolated and purified nucleic acid encoding an MCIP1 polypeptide lacking residues 1-80 of SEQ ID NO:2.
96. The nucleic acid of claim 95, further comprising a promoter.
97. The nucleic acid of claim 95, wherein said promoter is a muscle specific promoter.
98. The nucleic acid of claim 97, wherein said muscle specific promoter is myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na<sup>+</sup>/Ca<sup>2+</sup> exchanger promoter, dystrophin promoter, creatine kinase promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, and alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter and atrial natriuretic factor promoter.
99. An isolated and purified MCIP1 polypeptide lacking amino acid residues corresponding to Exons 1, 2 and 3.
100. An isolated and purified MCIP1 polypeptide lacking residues 1-80 of SEQ ID NO:2.

101. A method of treating cardiac hypertrophy or heart failure comprising administering to a subject suffering from cardiac hypertrophy or heart failure an agent that inhibits MCIP binding to calcineurin.

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